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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,043	04/03/2000	BERND EIKMANNS	21437	6651
535	7590	03/17/2006	EXAMINER	
THE FIRM OF KARL F ROSS 5676 RIVERDALE AVENUE PO BOX 900 RIVERDALE (BRONX), NY 10471-0900			STEADMAN, DAVID J	
		ART UNIT		PAPER NUMBER
				1656

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/529,043	EIKMANNS ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 02 December 2005.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 91-118 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) 91-108 is/are allowed.
- 6) Claim(s) 109-118 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                                          |                                                                                                |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                              | 4) <input type="checkbox"/> Interview Summary (PTO-413)                                        |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                     | Paper No(s)/Mail Date. _____ .                                                                 |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                    |
|                                                                                                                          | 6) <input checked="" type="checkbox"/> Other: <u>APPENDIX A</u><br><i>(Sequence alignment)</i> |

## **DETAILED ACTION**

### ***Status of the Application***

- [1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.
- [2] Claims 91-118 are pending in the application.
- [3] Applicant's amendment to the claims, filed on 12/2/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [4] Applicant's arguments filed on 12/2/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [5] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

### ***Claim Objection***

- [6] Claim 110 is objected to as there is a period after "wherein said" in line 4 of part b), which prematurely ends the claim. Appropriate correction is required.

***Claim Rejection - 35 USC § 112, Second Paragraph***

[7] Claims 109-118 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claim 109 is indefinite in the recitation of "substantially identical to...SEQ ID NO:2" as it is unclear from the specification and the claims as to how identical to SEQ ID NO:2 a sequence must be to be included within the scope of the claim. In the interest of advancing prosecution, the examiner has interpreted "substantially identical" to mean a sequence that has greater than 50% identity to SEQ ID NO:2. It is suggested that applicant clarify the meaning of the term "substantially identical" as it relates to SEQ ID NO:2.

[b] Claim 110 (claims 111-115 dependent therefrom) is confusing in the recitation of "aspartate and glutamate family strains.." as it is unclear as to the intended meaning of an aspartate and glutamate family strain. It is suggested that applicant clarify the meaning of the term.

[c] Claims 110 (claims 111-115 dependent therefrom) and 116 (claims 117-118 dependent therefrom) recite the limitation "the starting microorganism." There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejection - 35 USC § 112, First Paragraph***

[8] The new matter rejection of claim 109 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the term "substantially" is supported by the specification at p. 8, line 7. However, this is not found persuasive because the disclosure at p. 8, line 7 of the specification is related to a DNA sequence and not a polypeptide. It is suggested that applicant show support for the limitation of "substantially identical to...SEQ ID NO:2."

[9] The scope of enablement rejection of claim 109 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicants argue the rejection is obviated by amendment.

Applicant's argument is not found persuasive. At least for the reasons of record, which are based on a determination by weighing all of the factual considerations of In re Wands, it is the examiner's position that the specification does not enable the claimed invention without undue experimentation.

[10] Claims 110-112 and 116-118 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 110 (claims 111-112 dependent therefrom) and 116 (claims 117-118 dependent therefrom) are drawn to methods using a genus of transformed microorganisms that have increased “copy numbers” of pyruvate carboxylase.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the genus of recited transformed microorganisms, i.e., a microorganism transformed with an expression

vector comprising a nucleic acid encoding SEQ ID NO:2. Other than this single disclosed species, the specification fails to disclose any additional species of the recited genus of transformed microorganisms, which encompasses widely variant species because the microorganism can have increased "copy numbers" of pyruvate carboxylase by *any* modification, including, e.g., modification to endogenous promoter sequences, enhancer elements, and overexpressing transcription factors that regulate expression of pyruvate carboxylase.

Given the lack of description of a representative number of modified bacteria, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[11] Claims 110-112 and 116-118 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practicing the claimed methods using a microorganism transformed with an expression vector comprising a nucleic acid encoding SEQ ID NO:2, does not reasonably provide enablement for the claimed methods using any microorganism as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are so broad as to encompass the use of any microorganism having *any* modification that results in increased "copy numbers" of pyruvate carboxylase

including, e.g., modification to endogenous promoter sequences, enhancer elements, and overexpressing transcription factors that regulate expression of pyruvate carboxylase. The specification discloses only a single working example of such transformed microorganisms, i.e., a microorganism transformed with an expression vector comprising a nucleic acid encoding SEQ ID NO:2. Other than this single working example, the specification fails to provide any additional guidance for modifying a microorganism an expectation of achieving increased “copy numbers” of pyruvate carboxylase. The effects of modifying a microorganism with an expectation that the microorganism maintains the desired activity/utility is *highly* unpredictable. Because the specification fails to provide the necessary guidance, the experimentation required to make the full scope of recited transformed microorganisms is not routine. Thus, in view of the broad scope of the claims, the lack of guidance and working examples, the high level of unpredictability, and the amount of non-routine experimentation required, it is the examiner’s position that undue experimentation is required for a skilled artisan to make the full scope of recited microorganisms to practice the claimed methods.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

[12] Claim 109 is rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Accession Number P95127 (May 1, 1997). Claim 109 is drawn to an isolated pyruvate carboxylase polypeptide that has an amino acid sequence that is "substantially identical" to SEQ ID NO:2.

P95127 teaches a pyruvate carboxylase polypeptide that is 64.2% identical to SEQ ID NO:2 herein (see Appendix A). This anticipates claim 109 as written.

### ***Conclusion***

[13] Status of the claims:

Claims 91-118 are pending.

Claims 91-108 appear to be in a condition for allowance.

Claims 109-118 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.  
Primary Examiner  
Art Unit 1656

Art Unit: 1656

**APPENDIX A**

P95127\_MYCTU

ID P95127\_MYCTU PRELIMINARY; PRT; 1127 AA.

AC P95127; Q7D6C5;

DT 01-MAY-1997 (TrEMBLrel. 03, Created)

DT 01-MAY-1997 (TrEMBLrel. 03, Last sequence update)

DT 13-SEP-2005 (TrEMBLrel. 31, Last annotation update)

DE PROBABLE PYRUVATE CARBOXYLASE PCA (PYRUVIC CARBOXYLASE) (EC 6.4.1.1)

DE (Pyruvate carboxylase) (EC 6.4.1.1).

GN Name=pca; OrderedLocusNames=MT3045, Rv2967c;

OS Mycobacterium tuberculosis.

OC Bacteria; Actinobacteria; Actinobacteridae; Actinomycetales;

OC Corynebacterineae; Mycobacteriaceae; Mycobacterium;

OC Mycobacterium tuberculosis complex.

OX NCBI\_TaxID=1773;

RN [1]

RP NUCLEOTIDE SEQUENCE.

RC STRAIN=H37Rv;

RX MEDLINE=98295987; PubMed=9634230; DOI=10.1038/31159;

RA Cole S.T., Brosch R., Parkhill J., Garnier T., Churcher C.M.,

RA Harris D.E., Gordon S.V., Eiglmeier K., Gas S., Barry C.E. III,

RA Tekaiia F., Badcock K., Basham D., Brown D., Chillingworth T.,

RA Connor R., Davies R.M., Devlin K., Feltwell T., Gentles S., Hamlin N.,

RA Holroyd S., Hornsby T., Jagels K., Krogh A., McLean J., Moule S.,

RA Murphy L.D., Oliver S., Osborne J., Quail M.A., Rajandream M.A.,

RA Rogers J., Rutter S., Seeger K., Skelton S., Squares S., Squares R.,

RA Sulston J.E., Taylor K., Whitehead S., Barrell B.G.;

RT "Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence.";

RL Nature 393:537-544(1998).

RN [2]

RP NUCLEOTIDE SEQUENCE.

RC STRAIN=CDC 1551 / Oshkosh;

RX MEDLINE=22206494; PubMed=12218036;

RX DOI=10.1128/JB.184.19.5479-5490.2002;

RA Fleischmann R.D., Alland D., Eisen J.A., Carpenter L., White O.,

RA Peterson J.D., DeBoy R.T., Dodson R.J., Gwinn M.L., Haft D.H.,

RA Hickey E.K., Kolonay J.F., Nelson W.C., Umayam L.A., Ermolaeva M.D.,

RA Salzberg S.L., Delcher A., Utterback T.R., Weidman J.F., Khouri H.M.,

RA Gill J., Mikula A., Bishai W., Jacobs W.R. Jr., Venter J.C.,

RA Fraser C.M.;

RT "Whole-genome comparison of Mycobacterium tuberculosis clinical and laboratory strains.";

RL J. Bacteriol. 184:5479-5490(2002).

DR EMBL; BX842581; CAB05410.1; -; Genomic\_DNA.

DR EMBL; AE000516; AAK47371.1; -; Genomic\_DNA.

DR PIR; D70671; D70671.

DR HSSP; P02905; 1A6X.

DR HSSP; P24182; 1BNC.

DR TIGR; MT3045; -.

DR Tuberculist; Rv2967c; -.

DR GO; GO:0005737; C:cytoplasm; IEA.

DR GO; GO:0005524; F:ATP binding; IEA.

DR GO; GO:0009374; F:biotin binding; IEA.

DR GO; GO:0016874; F:ligase activity; IEA.

DR GO; GO:0004736; F:pyruvate carboxylase activity; IEA.

DR GO; GO:0006094; P:gluconeogenesis; IEA.

DR GO; GO:0008152; P:metabolism; IEA.

DR InterPro; IPR011761; ATP\_GRASP.

DR InterPro; IPR011764; BC.

DR InterPro; IPR001882; Biotin\_BS.

DR InterPro; IPR005482; Biotin\_carb\_C.

DR InterPro; IPR000089; Biotin\_lipooyl.

DR InterPro; IPR005481; CPase\_L\_N.

DR InterPro; IPR005479; Cphp\_synth\_L\_D2.

Art Unit: 1656

DR InterPro; IPR003379; PYC\_OADA.  
 DR InterPro; IPR005930; Pyruv\_carbox.  
 DR InterPro; IPR000891; PYR\_CT.  
 DR InterPro; IPR000634; S/T\_dehydrtse\_BS.  
 DR Pfam; PF02785; Biotin\_carb\_C; 1.  
 DR Pfam; PF00364; Biotin\_lipoyl; 1.  
 DR Pfam; PF00289; CPSase\_L\_chain; 1.  
 DR Pfam; PF02786; CPSase\_L\_D2; 1.  
 DR Pfam; PF00682; HMGL-like; 1.  
 DR Pfam; PF02436; PYC\_OADA; 1.  
 DR TIGRFAMs; TIGR01235; pyruv\_carbox; 1.  
 DR PROSITE; PS50975; ATP\_GRASP; 1.  
 DR PROSITE; PS50979; BC; 1.  
 DR PROSITE; PS00188; BIOTIN; 1.  
 DR PROSITE; PS50968; BIOTINYL\_LIPOYL; 1.  
 DR PROSITE; PS00867; CPSASE\_2; UNKNOWN\_1.  
 DR PROSITE; PS00165; DEHYDRATASE\_SER\_THR; UNKNOWN\_1.  
 DR PROSITE; PS50991; PYR\_CT; 1.  
 KW Complete proteome; Ligase; Pyruvate.  
 SQ SEQUENCE 1127 AA; 120422 MW; 84B0A4CC1A23CD90 CRC64;  
  
 Query Match 64.2%; Score 3712.5; DB 2; Length 1127;  
 Best Local Similarity 64.4%; Pred. No. 8.5e-193;  
 Matches 730; Conservative 153; Mismatches 239; Indels 11; Gaps 6;  
  
 Qy 12 FKKILVANRGEIAVRAFRALETGAATVAIYPREDRGSFHRSFASEAVRIGTEGSPVKAY 71  
 | : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 2 FSKVLVANRGEIAIRAFRAAYELGVGTAVYPYEDRNSQHRLKADESYQIGDIGHPVHAY 61  
  
 Qy 72 LDIDEIIGAAKKVKADAIYPGYGFLENAQLARECAENGITFIGPTPEVLDLTGDKSRAV 131  
 | : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 62 LSVDEIVATARRAGADAIYPGYGFLENAACAAAGISFVGPSAEVLELAGNKSRAI 121  
  
 Qy 132 TAAKKAGLPVLAESTPSKNIDEIVKSAEGQTYPIFKAVAGGGGRGMRFVASPDELRKLA 191  
 ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 122 AAAREAGLPVLMSSAPSASVDELLSVAAGMPFFLVFKAVAGGGGRGMRRVGDIALPEAI 181  
  
 Qy 192 TEASREAAAFGDGAVYVERAVINPQHIEVQILGDHTGEVVHLYERDCSLQRRHQKVVEI 251  
 ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 182 EAASREAEASAFGDPTVYLEQAVINPRHIEVQILADNLGDIVHLYERDCSVQRRHQKVIEL 241  
  
 Qy 252 APAQHLDPELRDRICADAVKFCRSIGYQGAGTVFVDEKGHNHVFIEMNPRIQVEHTVTE 311  
 ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 242 APAPHLDALERLYKMCVDAVAFARHIGYSCAGTVEFLDERGEYVFIEMNPRVQVEHTVTE 301  
  
 Qy 312 EVTEVDLVKAQMRLAAGATLKEGLTQDKIKTHGAALQCRTTEDPNNGFRPDTGTITAY 371  
 | : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 302 EITDVDLVSQLRIAGETLEQLGLRQEDIAPHGAALQCRTTEDPANGFRPDTGRISAL 361  
  
 Qy 372 RSPGGAGVRLDGAAQLGGEITAHDSDLVVKMTCRGSDFETAVARAQRALAEFTVSGVATN 431  
 | : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 362 RTAGGAGVRLDGSTNLGAEISPYFDSDLVVKLTCRGRDLPTAVSRARRAIAEFRIGVSTN 421  
  
 Qy 432 IGFLRALLREEDFTSKRIATGFIADHPHLQAPPADDEQGRILDYLADTVNKPHGVRPK 491  
 | : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 422 IPFLQAVLDDPDFRAGRVTTSFIDERPQLLTARASADRGTKILNFLADTVNNPYGSRPS 481  
  
 Qy 492 DVAAPIDKLPNIKDLPL---PRGSRDRLKQLGPAAFARDLREQDALAVTDTTFRDAHQ 547  
 : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 482 TI-YPDDKLP---DLDDLRAAPPAGSKQRLVKGPEGFARWLRESAAVGVTDTTFRDAHQ 537  
  
 Qy 548 LLATRVRSFALKPAAEAVAKLTPELLSVEAWGGATYDVAMRFLFEDPWDRLDELREAMPN 607  
 | : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||  
 Db 538 LLATRVRTSGLSRVAPYLARTMPQLLSVECWGGATYDVALRFLKEDPWERLATLRAAMPN 597  
  
 Qy 608 VNIQMLLRGRNTVGYPYDSCVCRASFVKEAASSGVDFRIFDALNDVSQMRPAIDAVLET 667  
 : : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||

Art Unit: 1656

Db 598 ICLQMLLGRNRTVGYTPYPEIVTSASFVQEATATGIDIFRIFDALNNIESMRPAIDAVRET 657  
Qy 668 NTAVAEVAMAYSGDLSDPNEKLYTLDYVLKMAEEIVKSGAHLAIKDMAGLLRPAAVTKL 727  
Db 658 GSAIAEVAMCYTGDLTDPGEQLYTLDYVLKLAEQIVDAGAHVLAIKDMAGLLRPAAQRL 717  
Qy 728 VTALRREFDLPVHVHTHDTAGGQLATYFAAAQAGADAVDGASAPLSGTTSQPSLSAIVAA 787  
Db 718 VSALRSRFDLPLVHLHTHDTPGQLASYVAAWHAGADAVDGAAAPLAGTTSQPALSSIVAA 777  
Qy 788 FAHTRRDGTGLSLEAVSDLEPYWEAVRGLYLPFESGTPGPTGRVYRHEIPGGQLSNLRAQA 847  
Db 778 AAHTEYDTGLSLSAVCALLEPYWEALRKVYAPFESGLPGPTGRVYHHEIPGGQLSNLRQQA 837  
Qy 848 TALGLADRFLIEDNYAAVNEMLGRPTKVTPSSKVVGDLALHLVGAGVDPADFAADPQKY 907  
Db 838 IALGLGDRFEEIEEAYAGADRVLGRLVKVTPTSKVVGDLALALVGAGVSADEFASDPARF 897  
Qy 908 DIPDSVIAFLRGELGNPPGGWPEPLRTRALEGSEGKAPLTVEPVEEQAHLDADDSKERR 967  
Db 898 GIPESVILGFLRGELGDPPGGWPEPLRTAALAGRGAAR-PTAQLAADDEIALSSVGAK-RQ 955  
Qy 968 NSLNRLLFPKPTEEFLEHRRRGNTSALDDREFFYGLVEGRETLIRLPDVRTPLLVRLDA 1027  
Db 956 ATLNRLLFPSPTKEFNEHREAYGDTSQLSANQFFYGLRQGEEHRVKL-ERGVELLIGLEA 1014  
Qy 1028 ISEPDDKGMRNVVANVNGQIRPMRVRDRSVESVTATAEKADSSNKGHVAAPFAGVVTVT 1087  
Db 1015 ISEPDERGMRTVMCILNGQLRPVLVRDRSIASAVPAAEKADRGNPGHIAAPFAGVVTVG 1074  
Qy 1088 AEGDEVKAGDAVIIIEAMKMEATITASVDGKIDRVVVPAATKVEGGDLIVVVS 1140  
Db 1075 CVGERVGAGQTIATIEAMKMEAPITAPVAGTVERVAVSDTAQVEGGDLLVVVS 1127